

WHAT IS CLAIMED IS:

1. A method for cleavage of a linker from an oligonucleotide, comprising contacting a conjugate comprising an oligonucleotide, a linker and a solid support with a gaseous nucleophilic composition under conditions that result in the cleavage of the linker from the oligonucleotide.
2. The method of claim 1, wherein said linker is a universal linker.
3. The method of claim 1, wherein said linker which attaches the oligonucleotide to the solid support is not the 3'-terminal nucleotide.
4. The method of claim 1, wherein the linkage being cleaved is an ester linkage between the 3'-OH of the oligonucleotide and phosphate of the linker.
5. The method of claim 4, wherein the linker, when removed, produces a phosphorous containing heterocycle.
6. The method of claim 1, wherein said linker contains 2 vicinal heteroatoms.
7. The method of claim 1, wherein said linker comprises a vicinal diol.
8. The method of claim 1, wherein said linker comprises a vicinal amino alcohol.
9. The method of claim 1, wherein said linker comprises a vicinal thiol alcohol.

10. The method of claim 1, wherein said gaseous nucleophilic compound is ammonia vapors.

11. The method of claim 1, wherein said gaseous nucleophilic compound is hydrated ammonia vapors.

12. The method of claim 1, wherein said conditions comprise carrying out the process for about 1 minute to 240 minutes.

13. The method of claim 11, wherein said conditions comprise carrying out the process for about 60 minutes.

14. The method of claim 1, wherein said conditions comprise carrying out the process at about room temperature to about 150°C.

15. The method of claim 14, wherein said conditions comprise carrying out the process at about 95°C.

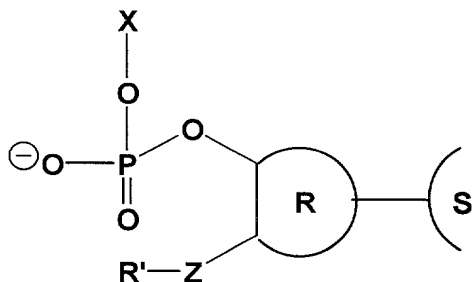
16. The method of claim 1, wherein said the ester linkage between the 3'-hydroxyl of the terminal nucleotide of the oligonucleotide and the linker is substantially cleaved.

17. The method of claim 16, wherein said cleaved oligonucleotide is recovered by washing said solid phase with water or aqueous buffer.

18. A method for cleavage of a linker from an oligonucleotide, comprising contacting ammonium hydroxide vapors with a conjugate comprising a linker, an oligonucleotide and a solid support at 95°C and 80 psi for 120 minutes, resulting in the cleavage of the linker from the oligonucleotide.

00965750-43594

19. The method of claim 1, wherein the oligonucleotide, linker, solid support conjugate has the formula:



wherein X is the termini of the oligonucleotide, S is a solid support, R is an optionally substituted tetrahydrofuran, phenyl or cyclopentane ring, and R' is a protecting group, and Z is O, S or Se.

20. The method of claim 19, wherein X is the 3' terminal nucleotide of the oligonucleotide.

21. Method of claim 19, wherein the protecting group is a DMTr, acyl, aryl, silyl, tripluoroacetyl, benzyl, substituted benzyl or aryl group.